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L4: Entry 3 of 3 File: USPT Feb 10, 1998

DOCUMENT-IDENTIFIER: US 5716825 A
TITLE: Integrated nucleic acid analysis system for MALDI-TOF MS

DEPR:
The advantage of integrating the sample preparation compartment with the MALDI ionization surface is to allow automated chemical manipulation of analytical samples prior to analysis by MALDI-TOF MS without manual sample handling, thus reducing contamination and sample loss while allowing specific chemical pretreatment prior to MALDI analysis to enhance the selectivity, sensitivity and/or reproducibility of the measurements. This feature will be of particular importance if the full sensitivity of MALDI-TOF is to be achieved. With particular reference to the present invention, the integration of a miniaturized nucleic acid analysis system, having the capability of amplifying small amounts of oligonucleotide analytes, with MALDI-TOF MS is intended to provide a highly sensitive, accurate, rapid, and reproducible technique for detecting and elucidating the structure of oligonucleotides present in relatively small quantities in clinical and forensic samples. The sensitivity of detection (between 10.sup.-12 to 10.sup.-15 moles of oligonucleotide deposited on a MALDI ionization surface) means that an oligonucleotide analyte need not be amplified to the same extent as is required for other analytical techniques, while the speed of measurement (on the order of a few minutes) should facilitate the performance of multiple mass determinations in a single experiment. The use of disposable probes is intended to minimize sample contamination.

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L11: Entry 1 of 2 File: USPT Nov 16, 1999

DOCUMENT-IDENTIFIER: US 5985619 A
TITLE: Use of exonuclease and/or glycosylase as supplements to anti-polymerase antibody to increase specificity in polymerase chain reaction

DRPR:
The glycosylases useful in the present invention are those that specifically cleave unconventional bases, i.e., bases other than A, G, C or T in DNA and A, G, C and U in RNA. In embodiments of the present invention utilizing a glycosylase, the appropriate deoxyribonucleoside triphosphate for which the glycosylase is specific is substituted for the corresponding conventional dNTP. Glycosylases that specifically cleave unconventional bases such as N-7 methylguanine, 3-methyladenosine, uracil and hypoxanthine are known to one of ordinary skill in the art and described, for example, in PCT/US91/05210 to Sninsky St A. Preferred glycosylases include uracil N-glycosylase (UNG), hypoxanthine-DNA glycosylase, and 3-methyadenine-DNA glycosylases I and II. The most preferred glycosylase in accordance with the present invention is UNG. UNG is commercially available (Perkin-Elmer). UNG catalyzes the excision of uracil from single or double-stranded DNA. In embodiments of the present invention utilizing UNG, the deoxyribonucleoside triphosphate dUTP is substituted for dTTP so that dUTP is incorporated into amplification products. Because UNG is inactivated by temperatures used in thermal cycling, UNG attacks only uracil containing DNA that is produced prior to thermal cycling, i.e., at zero cycle. The abasic polynucleotides resulting from UNG cleavage cannot function as PCR templates. (Longo et al. (1990) Gene 93:125).